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# Reviews/Analyses

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## Strategies for minimizing nosocomial measles transmission\*

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*As a result of the highly contagious nature of measles before the onset of rash, nosocomial transmission will remain a threat until the disease is eradicated. However, a number of strategies can minimize its nosocomial spread. It is therefore vital to maximize awareness among health care staff that an individual with measles can enter a health facility at any time and that a continual risk of the nosocomial transmission of measles exists. The present review makes two groups of recommendations: those which are generally applicable to all countries, and certain additional recommendations which may be suitable only for industrialized countries.*

### Introduction

In the first decade of the 21st century, measles may well be the next disease after smallpox, poliomyelitis, and dracunculiasis to be targeted for global eradication. However, until eradicated, measles remains a threat, especially to children admitted to health care facilities.

The contribution of nosocomial transmission to the incidence of measles varies considerably, according to the prevailing measles epidemiology in an area. Several studies have demonstrated that nosocomial transmission is important in industrialized countries and in urban settings in developing countries. However, such transmission probably does not contribute significantly to measles incidence in rural communities in developing countries, where immunization coverage remains low to moderate and access to health facilities or their use by community members for diseases such as measles is limited.

Until measles is eradicated it will be difficult to eliminate its nosocomial transmission because of certain limiting factors, including the highly contagious nature of the disease in the incubation phase. However, several strategies can minimize such transmission. It is therefore vital to raise awareness among health care staff that an individual with measles can enter a health facility at any time, so that personnel remain alert to the risk of spread to non-immune persons.

Measles is caused by one of the most infectious human pathogens, and is certainly the most contagious vaccine-preventable disease. This is the result of the virus's ability to remain viable for extended periods of time in small droplets expelled by infected individuals on coughing (1-3). Measles transmission is therefore facilitated by the collection of susceptible individuals in confined spaces where such infectious aerosols linger.

Outside the home, high-risk settings include educational facilities, sports halls, religious institutions, orphanages, refugee camps, and health facilities (4, 5). Health facilities are of particular concern because of the risk of exposure to measles for those who may already be seriously ill. The use of a sterile syringe for every immunization or therapeutic injection will ensure that the infection is not spread by this route, but such precautions do nothing to prevent aerosol transmission.

This article reviews relevant literature, where possible quantifies the contribution of nosocomial transmission to the overall incidence of measles, and provides practical recommendations for strategies to minimize nosocomial transmission.

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## Epidemiology of nosocomial measles

Where measles virus circulates in a community, it is likely to be a common pathogen in health facilities, and a significant proportion of individuals may acquire the infection while visiting a health facility. A study of nosocomial infection conducted during 1946–47 in 26 children's wards in 14 representative hospitals throughout the United Kingdom found that 12% of all nosocomial infections were measles (6). A similar finding was reported among black children of low socioeconomic class admitted to a major teaching hospital in South Africa in 1987 (7). These studies may in fact have underestimated the proportion of nosocomial infections due to mea-

sles since post-discharge surveillance was not always performed.

The relative contribution of nosocomial transmission to the overall incidence of measles appears to vary in accordance with prevailing measles epidemiology (Table 1). Analysis of published data suggests an increasing trend for the proportion of nosocomially acquired cases in certain settings.

Published national surveillance data are available for the USA for 1980–90, where high vaccination coverage had reduced measles incidence to historically low levels and the majority of reported cases were associated with isolated outbreaks (8). Information on the probable source of exposure was, on average, available for half of the reported cases. Of these, <10% were reported as infected in health

Table 1: **Relative contribution of nosocomial transmission to measles incidence in industrialized and developing countries**

Country	Year	% cases associated with nosocomial spread	Author, publication year (ref.)
<b>Industrialized countries</b>			
<i>National surveillance</i>			
USA	1980	0.4	CDC, <sup>a</sup> 1981 (41)
USA	1981	1.1	Davis et al., 1986 (40)
USA	1982	1.2	Davis et al., 1986 (40)
USA	1983	3.7	Davis et al., 1986 (40)
USA	1984	2.5	Davis et al., 1986 (40)
USA	1985	4.7	CDC, 1986 (42)
USA	1987	5.8	CDC, 1989 (43)
USA	1989–90	9.0	Gindler et al., 1992 (5)
<i>Outbreak investigations (community-based)</i>			
USA (OK)	1981–85	27	Istre et al., 1987 (11)
USA (CA)	1983	29	Dales et al., 1985 (10)
USA (HI)	1984	15	CDC, 1984 (9)
<i>Outbreak investigations (health facility-based)</i>			
France	1983–84	16	Foulon et al., 1986 (38)
USA (MI)	1985	57	Sienko et al., 1987 (15)
USA (NM)	1986	43	CDC, 1987 (13)
South Africa	1985–86	25	Reynolds et al., 1987 (14)
USA (MI)	1990	48	McGrath et al., 1992 (16)
USA (CA)	1990	72	Mason et al., 1993 (17)
<i>Case-control</i>			
USA (CA)	1988–89	23 <sup>b</sup>	Farizo et al., 1991 (18)
USA (TX)	1988–89	41 <sup>b</sup>	Farizo et al., 1991 (18)
<b>Developing countries</b>			
<i>Outbreak investigations (community-based)</i>			
Brazil	1983	21	PAHO, <sup>c</sup> 1984 (19)
<i>Outbreak investigations (health facility-based)</i>			
Cameroon	1975	35	Guyer, 1976 (20)
Mozambique	1980	33	Rabelo, 1982 (45)
Guinea-Bissau	1980–82	16	Aaby et al., 1985 (21)
<i>Case-control</i>			
Côte d'Ivoire	1985	71 <sup>b</sup>	Klein-Zabban et al., 1987 (23)
Burundi	1988	32	Chen, 1990 (24)

<sup>a</sup> CDC = Centers for Disease Control and Prevention.

<sup>b</sup> Significantly more cases than controls (46 of 64 compared with none of 21;  $P < 0.1$ ) had visited a health facility during the 2 weeks prior to the onset of rash among cases.

<sup>c</sup> PAHO = Pan American Health Organization.

facility settings during this period. However, our review of published data suggests that nosocomial transmission in the USA, as a proportion of all transmission, increased by a factor of 20, in a roughly linear fashion, across the same period. Although these data are potentially biased (a large proportion of cases had no reported source of exposure), it is unlikely that bias alone would explain the marked trend observed in the proportion of nosocomial spread.

Data derived from measles outbreak investigations in three industrialized countries (France, South Africa, and the USA), show the proportion of cases with exposure in health facility settings to range from 15% to 72%. This proportion was generally lower in community-based studies (9–11) than in studies of urban health-facility-based outbreaks or hospitalized cases (12–17). This is as expected, since facility-based studies tend to over-represent community members who make greater use of health facilities, and therefore tend to overestimate the community infection rate. Case-control studies performed in the USA of measles transmission in Los Angeles and Houston showed that attendance at a hospital emergency room 10–18 days prior to the onset of measles rash was a significant risk factor (18).

Among data from measles outbreak investigations in six developing countries (Brazil, Burundi, Cameroon, Côte d'Ivoire, Guinea-Bissau, and Mozambique), the proportion of measles cases with exposure in health facility settings ranged from 21% to 71%. The proportion of cases associated with nosocomial spread was generally similar in a community-based study (19) in Brazil and in studies of urban health-facility-based outbreaks or hospitalized patients (20, 21). A case-control study performed in Abidjan showed that attendance at a hospital emergency room up to 2 weeks previously (the approximate incubation period for measles) was a significant risk factor for acquiring measles (22, 23). However, a study in a rural area of Burundi found no difference in the proportion of cases and controls visiting a health facility during the previous month (24). A community-based study in Burundi found that only 1% of those with measles had visited a health facility during the previous month.

In sum, these studies suggest that nosocomial transmission is important in industrialized countries and in urban settings in developing countries. Further, data from the USA suggest that the relative contribution of nosocomial transmission will increase as high vaccination coverage rates are achieved in more countries (25) and endemic (non-outbreak) measles declines in importance. These studies also suggest that nosocomial transmission does not contribute significantly to measles incidence in rural communities in developing countries

where vaccination coverage remains low to moderate and where access to health facilities or their utilization by community members for diseases like measles is limited.

## Factors influencing the control of nosocomial measles

### *Characteristics of transmission*

Measles is an acute, highly contagious disease transmitted by direct contact with infectious droplets (26). Immunity from the disease is lifelong; seroconversion following successful immunization is also for all practical purposes lifelong.

The virus is secreted in the nasopharynx of sick individuals and expelled in aerosolized droplets on coughing. Several studies have demonstrated that infection can occur without face-to-face contact with a contagious individual. Measles transmission has been documented even when the contagious person has left the room up to 2 hours before the arrival of those subsequently acquiring infection (1, 3, 9, 13, 15, 27–29). In a U.S. high school, one child with a vigorous cough caused an explosive single-generation measles epidemic among 69 non-immune children, many of whom had no direct contact with the index case but shared the same corridors between classes (29).

Since measles patients are contagious from 3–5 days before the onset of rash (1–2 days before the onset of fever and other symptoms), it can be difficult to identify infectious individuals, many of whom exhibit non-specific symptoms. Such patients facilitate nosocomial transmission and complicate its control.

### *Age of patients and disease severity*

Measles transmission is facilitated by human proximity and crowding (30), such as occurs in busy health clinics. In addition, there is an increased risk of severe measles in crowded conditions, such as occur in developing countries (31–36). Indeed, crowding (which is a proxy for the intensity of the viral dose) appears to be more important than nutritional status (a proxy for host resistance) in determining the severity of disease (33, 35). Other studies have shown that complication rates and case-fatality rates were significantly higher, and recovery times longer, in infants and young children acquiring measles nosocomially, compared with those acquiring it in the community (14, 37–39).

In the USA during 1983–84, 20% of measles cases occurred in infants and children too young to

have been eligible for vaccination, whereas 59% of those with nosocomially acquired measles were ineligible (40). Infants and young children may be at greater risk of nosocomial acquisition because of more frequent visits to medical facilities, for example for immunization and well-baby clinics.

### **Characteristics of health facilities**

Health facilities play an important role in measles transmission, not only within their walls but also to the whole community, in both industrialized countries (1, 3, 5, 9, 11, 13–18, 28, 38, 40–43) and developing countries (7, 19–21, 23, 24, 38, 44, 45). A 5-year retrospective study in the USA during the early 1980s implicated all types of health care settings; the greatest proportions of nosocomially acquired measles infections were in hospitals (47%), physicians' offices (35%), and outpatient clinics (15%) (40). During community-wide measles outbreaks in two cities in the USA, visiting a hospital emergency room 10–18 days prior to the onset of measles rash was a significant risk factor (19). Measles transmission also occurred in pharmacies, nonhospital emergency centres, a drug rehabilitation centre, and a laboratory. A total of 45% of measles cases evaluated in another study in the USA resulted either directly or indirectly from exposure in medical waiting rooms (11). In developing countries, maternal and child health care clinics have been implicated in the nosocomial spread of measles (20, 38). Studies of measles outbreaks in the USA revealed that low relative humidity and a lack of fresh-air circulation in waiting rooms seem to facilitate measles transmission (3).

### **The role of health care staff**

While most nosocomially spread outbreaks of measles involve non-immune patients and visitors, non-immune health workers are often involved, especially in countries where measles has not been endemic for many years (46–51). The above-mentioned 5-year retrospective study in the USA during the early 1980s revealed that, among nosocomially transmitted measles cases, 50% were transmitted patient-to-patient, 37% patient-to-staff, 8% patient-to-visitor, 3% staff-to-staff, and 2% staff-to-patient (40). Staff acquiring measles most frequently were those who had contact with patients or laboratory specimens, including nurses, physicians, laboratory technicians, and clerk/receptionists. In contrast to industrialized countries, many health care workers in developing countries grew up before measles vaccination was widespread, are therefore likely to be immune from exposure (usually in childhood), and thus do not contribute to nosocomial transmission.

## **Prevention through vaccination**

If all infants and children were immune to measles before exposure to a contagious individual in a medical setting, nosocomial transmission could not occur. However, routine measles vaccination of infants 9 months of age or older will not protect susceptible infants under 9 months of age. Individuals who receive measles vaccine but fail to respond with protective levels of antibody will also not be protected. In addition, the ascertainment of measles vaccination status among infants and children, especially in developing countries, can be complicated by low rates of vaccination-card retention. The prevention of nosocomially acquired measles through pre-exposure vaccination therefore requires additional vaccination strategies.

Several studies have demonstrated that measles vaccine is effective in preventing the development of clinical measles in exposed individuals if vaccination is performed within 72 hours of exposure (52). The rate of protection varied between 68% and 100%. Four studies of household or institutional (including nosocomial) exposure reported protection rates of 94% or greater (59–62). However, the effectiveness of post-exposure prophylaxis among children under 1 year of age, particularly those less than 9 months of age, has not been studied. Nevertheless, these findings lend support to recommendations to vaccinate individuals against measles within 72 hours of exposure (26).

## **Recommendations for control**

Since measles is highly contagious during the pre-rash phase, it will be extremely difficult to eliminate its nosocomial transmission until the disease itself is eradicated. However, a number of strategies can minimize nosocomial spread. The following recommendations are divided into those which are applicable to all countries, and certain recommendations which may be suitable only for industrialized countries.

### **Measures applicable to all countries**

**Maintain a high level of awareness among staff.** It is vital to maximize awareness among health facility staff that an individual with measles can enter the facility at any time and that a continuous risk of the nosocomial spread of measles to non-immune persons exists.

**Maintain high coverage in the community.** The accumulation of susceptible individuals in the community will be minimized by maintaining high rates of mea-

sles vaccination coverage. Several strategies for achieving high coverage have been described (25). A combination may be required, including routine vaccination, special actions for high-risk groups or areas, and mass campaigns.

Since there are virtually no contraindications to measles vaccination, measles vaccine should be administered regardless of the patient's health status. Measles vaccination is particularly important for malnourished children and for those with chronic illnesses, as they are at increased risk of complications due to measles. An exception to this recommendation are children who, on admission, are so ill that they are at serious risk of dying. Although administration of measles vaccine is not dangerous in such cases, parents may incorrectly attribute a death to the vaccination.

**Reduce vaccination age during outbreaks.** WHO recommends that the age for administration of measles vaccine should be lowered to 6 months during outbreaks where high attack rates are anticipated. Vaccine should be administered any time after 6 months of age and, for infants vaccinated between 6 and 9 months of age, a second dose should be administered as soon as possible after 9 months of age, provided that at least 4 weeks have elapsed since the last dose of vaccine. The second dose after 9 months of age is important, as the serological response to vaccine given before 9 months of age may be significantly lower, resulting in lower levels of protection. Parents should receive appropriate instructions when an early dose is administered. (The recommendation for the re-vaccination of children vaccinated before 9 months of age also applies to the sections that follow.)

**Eliminate missed vaccination opportunities.** Missed opportunities for vaccination should be eliminated by routinely checking the measles vaccination status of all children attending any health facility for any reason. This should be implemented at all immunization clinics, physicians' offices, public and private clinics, health centres, and hospital emergency and outpatient wards. Even children with a history of measles disease should be vaccinated, as physicians, health care workers, mothers, and other caretakers occasionally mistake other fever and rash illnesses for measles. In addition, a verbal history of previous measles vaccination is insufficient to contraindicate vaccination—only vaccination card documentation should be accepted.

In developing countries, where vaccination cards or clinic records are often missing, local conditions should be evaluated when determining criteria for administering measles vaccine to children whose vaccination status cannot be verified. Where indi-

cated by epidemiological analysis, including the assessment of case-fatality rate, the response to measles outbreaks may include the vaccination of all children aged 6 or 9 months to 9 years of age, regardless of measles vaccination history. In the absence of an outbreak, it is recommended that all children aged 9 months to 2 years, at a *minimum*, without documented evidence of vaccination should receive measles vaccine.

A simple method is available for assessing the extent of missed vaccination opportunities (53). Systematic efforts should be made to eliminate all missed opportunities. Any child eligible for measles vaccine (or other antigens, and any woman eligible for tetanus toxoid) should receive any missing dose(s) before leaving a health facility. If a non-immune person is exposed to measles through direct or indirect contact with a contagious individual, measles vaccine will usually provide protection if administered within 72 hours of exposure.

**Ensure vaccination among hospitalized patients.** The vaccination status of all children admitted to hospital should be rigorously checked. WHO recommends that, in developing countries, a dose of measles vaccine should be given to all infants aged 6 months to 9 years (the age range to be adjusted in light of local conditions) upon admission to hospital, even if there is documented evidence of previous measles vaccination. In most industrialized countries, only patients who lack vaccination documentation need be vaccinated upon admission.

At best, measles vaccination is associated with an efficacy of 80–90% in developing countries (19, 54–57). Thus, an extra dose of vaccine upon admission to hospital can significantly reduce the likelihood of nosocomial measles transmission.

The vaccination status of hospitalized children should also be checked before they are discharged from hospital. Vaccination of those without documentation of previous measles vaccination reduces the chances of a child returning home while incubating a nosocomially acquired measles infection. Failure to do this could result in the infection of other children in the community.

Non-immune persons over 6 months of age who are exposed to measles patients in the hospital, such as patients sharing the same ward and visitors, should receive a dose of measles vaccine, wherever possible, within 72 hours of exposure. For patients who are not immunocompromised, the use of hyper-immune measles gamma globulin (IMGG) may be less effective and is more costly than measles vaccine.

**Isolate individuals with fever and rash.** To reduce the chance of exposure to measles, individuals with fever

and rash should preferably not enter the common waiting areas of a health facility. Wherever feasible, such patients should be fitted with a mask and taken directly to a room reserved for those with diseases subject to respiratory isolation. Moreover, if possible, waiting and treatment areas should be well ventilated, and, to the extent possible, care should be taken to ensure that sick and well children do not sequentially use the same room and are not dealt with by the same staff for weighings, clinical examinations, vaccinations, or other consultations, as this could clearly provide a vehicle for measles transmission. Where female literacy is common, a sign can be mounted outside health facilities instructing parents or guardians accompanying a child with fever and rash to wait outside and to ask another attendee to inform the health care staff that a sick child has arrived.

To reduce the severity of measles and the risk of subsequent complications, vitamin A supplements (200 000 IU on two successive days for those >1 year of age) should be administered to all hospitalized children with suspected measles.<sup>a</sup>

**Inform health authorities.** Measles is a reportable disease in almost all countries. Cases of measles should be reported promptly to the district health authorities in accordance with accepted local procedures. In addition, nosocomially acquired cases of measles should be reported immediately to the hospital's infection control authorities for investigation and response such as increased isolation precautions for sick children.

### **Control measures for industrialized countries**

**Ensure vaccination of health facility staff.** All health facility staff should be immune to measles. Most adults in developing countries will already have natural immunity. Particularly in industrialized countries, where some adults may not be immune, any staff member without documentary proof of measles vaccination or adequate measles antibody titres at the time of employment should receive measles vaccination, after screening for contraindications such as pregnancy or immune suppression.

**Administer gamma globulin to selected patients.** Since there is a risk of overwhelming viraemia, live viral vaccines such as measles vaccine are

contraindicated in individuals with congenital immune function disorders or those receiving immunosuppressive therapy. Hence, immunocompromised individuals coming into contact with measles patients should receive IMGG as soon as possible after exposure. However, persons seropositive for human immunodeficiency virus (HIV) or with suspected or confirmed acquired immunodeficiency syndrome (AIDS) can receive live measles vaccine (58).

## **Conclusions**

Until measles is eradicated, its nosocomial transmission remains a threat. Reducing through immunization the amount of virus circulating in the community remains the strategy of choice for combating measles. However, additional measures are available that will help reduce transmission of measles in the health care setting. These strategies include admission and discharge vaccination checks, vaccination of staff, and isolation of patients with fever and rash, particularly in epidemic situations. Strategies such as the triage of possible measles cases in hospital and health clinic waiting areas and engineering modifications to air flows, are potentially beneficial but are more difficult to implement and largely untested.

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## **Résumé**

### **Stratégies de réduction du risque de transmission nosocomiale de la rougeole**

Due à plusieurs facteurs comme la grande contagiosité de la maladie pendant la phase d'incubation — avant l'apparition des symptômes — la transmission nosocomiale de la rougeole constituera une menace tant que cette maladie n'aura pas été éliminée ou éradiquée. Il est cependant possible, grâce à diverses stratégies, de réduire sa propagation nosocomiale. Il est indispensable que le personnel de santé soit conscient qu'un malade atteint de rougeole peut se présenter dans un établissement de soins à tout moment et qu'il existe un risque permanent de transmission nosocomiale de cette maladie aux personnes non immunes.

Dès que le virus de la rougeole circule dans une communauté, il est probable qu'il devienne un agent pathogène courant dans les établissements

<sup>a</sup> See: *Using immunization contacts as the gateway to eliminating vitamin A deficiency: a policy document*. Geneva, World Health Organization, 1994 (unpublished document WHO/EPI/GEN/94.9 Rev. 1, available on request from Expanded Programme on Immunization, World Health Organization, 1211 Geneva 27, Switzerland).

de soins, et en fait une proportion notable des cas sont probablement contractés lors d'une visite dans un tel établissement. Bien que, globalement, moins de 10% des cas de rougeole pour lesquels une source probable d'exposition a été identifiée aient été déclarés comme contractés dans un établissement de soins aux Etats-Unis d'Amérique entre 1980 et 1990, l'examen des données publiées indique que la proportion de cas attribuables à une transmission nosocomiale a été multipliée par vingt, de façon pratiquement linéaire, pendant cette même période.

Une étude rétrospective de 5 ans réalisée aux Etats-Unis d'Amérique au début des années 80 a montré que tous les types d'établissements de soins étaient impliqués, la plus forte proportion de rougeoles nosocomiales étant contractée à l'hôpital (47%), dans un cabinet médical (35%) ou dans un dispensaire (15%). Lors des flambées d'ampleur communautaire, les agents de santé non immuns sont souvent en cause, surtout dans les pays où la rougeole n'a plus été endémique depuis de nombreuses années.

Les données rapportées indiquent donc que le contact nosocomial avec le virus est un important mécanisme de transmission de la rougeole dans les pays industrialisés et dans les secteurs urbains des pays en développement. En revanche, ce mode de transmission ne contribue peut-être pas de façon significative à l'incidence de la rougeole dans les communautés rurales des pays en développement où la couverture vaccinale est encore faible à moyenne et où l'accès aux établissements de soins ou leur utilisation par les membres de la communauté pour des maladies telles que la rougeole sont limités. Les données américaines suggèrent néanmoins que la contribution relative de la transmission nosocomiale à la propagation générale de la rougeole ira en augmentant à l'échelle mondiale, au fur et à mesure de l'amélioration de la couverture vaccinale dans de nombreux pays et du déclin de la rougeole endémique (survenant en dehors des épidémies).

Les recommandations relatives à la lutte contre la transmission nosocomiale de la rougeole se divisent en deux groupes, celles qui sont applicables dans tous les pays et certaines recommandations complémentaires qui peuvent n'être applicables que dans les pays industrialisés.

#### *Mesures de lutte applicables dans tous les pays*

- Maintenir un taux élevé de couverture vaccinale antirougeoleuse dans la communauté
- Eliminer systématiquement les occasions manquées de vaccination antirougeoleuse.

- Veiller à ce que les agents de santé aient parfaitement conscience du risque de transmission nosocomiale.
- Isoler dès leur arrivée les personnes qui se présentent à l'établissement de soins avec de la fièvre et une éruption cutanée.
- Vérifier l'état vaccinal de tous les malades, à l'admission et à la sortie de l'hôpital.
- Abaisser l'âge de la vaccination à 6 mois lors des épidémies où des taux d'atteinte élevés sont prévus.
- Déclarer les cas de rougeole aux autorités sanitaires.

#### *Mesures de lutte applicables uniquement dans les pays industrialisés*

- Veiller à ce que tous les agents de santé soient vaccinés contre la rougeole.
- Administrer des gammaglobulines antirougeoleuses hyperimmunes aux personnes immuno-déprimées exposées à la rougeole.

Tant que la rougeole ne sera pas éradiquée, la transmission nosocomiale restera une menace. Face à cette situation, la stratégie de choix consiste à réduire, grâce à la vaccination, la quantité de virus en circulation dans la communauté. Des mesures complémentaires peuvent cependant contribuer à réduire le risque de transmission de la maladie dans les établissements de soins. On peut ainsi vacciner les patients hospitalisés à l'admission et à la sortie, vacciner le personnel, et isoler les malades, en particulier en période d'épidémie. D'autres mesures, comme l'adoption de salles d'attente séparées pour les patients suspects de rougeole, et des aménagements des systèmes de circulation et de filtration de l'air, bien que d'un grand intérêt potentiel, sont plus difficiles à mettre en oeuvre et doivent encore être testées.

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